REMARKS

This paper cancels claims 13-15, without prejudice or disclaimer to the subject matter recited therein, and amends claim 1. Claims 1-12 remain in this application.

The above-detailed amendments to claim 1 incorporate the limitations of original claim 15 into claim 1. Applicants believe that entry of this amendment will place all claims in this case in condition for allowance, or will simplify the issues for appeal. Compliance with 37 CFR §1.116(b) is respectfully asserted, and entry and consideration of this amendment is requested.

The Examiner has rejected claims 1, 2, and 6-15 under 35 U.S.C. §103 as being unpatentable over the Anderson et al. reference taken with Brown et al. Applicants respectfully traverse this rejection.

First, the incorporation of the limitations of claim 15 into claim 1 now makes clearer that the radiation frequencies are selected in order to distinguish one constituent component of whole blood from another constituent component, in addition to being selected to minimize the effects of radiation scattering and to maximize radiation absorbance. As explained in the specification, for example with reference to the prior art Fig. 2, radiation scattering results in a highly nonlinear relationship existing between the optical density of whole blood and hemoglobin concentration. According to the present invention, the selection of the specific radiation frequencies, the control of sample depth,

and the placement and size of a radiation detecting area, all contribute to the minimization of the effects of radiation scattering by whole, undiluted blood thereby rendering substantially linear the functional relationship between optical density and hemoglobin concentration. This substantial linearity is illustrated in the graph of Fig. 5.

As explained in the present specification, this linearity allows application of Beer's law of absorption spectrometry to whole, undiluted blood, and for the first time allows the application of Beer's law to determine at least three constituent components of whole undiluted blood.

In addition, claim 1 now requires the radiation frequencies to be selected in order to distinguish one constituent blood component from another constituent component. As presented in the specification, for example at page 4, lines 14-23, and page 6, lines 15-32, this is accomplished by selecting radiation frequencies which minimize the sensitivity of the molar extinction coefficients to small variations in the radiation wavelength, and by choosing the radiation wavelength so that, for each wavelength, the molar extinction coefficient for at least one of the hemoglobin species under consideration is very large.

In contrast, in the Anderson et al. article, there is no suggestion to select radiation frequencies and optical geometry so that absorption is maximized and scattering is minimized, and there is no suggestion to select radiation frequencies to allow the discrimination between one constituent component and another.

The Anderson et al. reference deals with the general observation of light scattering and absorbance in whole, undiluted blood at various frequencies. However, there is no suggestion in Anderson et al. to select radiation frequencies where absorbance is maximized and scattering is minimized, and there is no suggestion in Anderson et al. to select radiation frequencies that promote discrimination of one blood component from another.

This is best illustrated by comparing the graph of Fig. 2 of Anderson et al. with the graph of Fig. 5 of the present specification, which both plot optical density against hemoglobin concentration at various radiation frequencies. While the present invention renders a substantially linear functional relationship, three out of the four wavelengths plotted in the Anderson et al. article produce highly nonlinear results (similar to Fig. 2 of the present specification), illustrating the deleterious effects of light scattering at these frequencies. Similar nonlinearities appear in Figs. 3 and 6 of the Anderson et al. article.

It is not clear from the Anderson et al. article whether they have failed to select properly the specific radiation frequencies, or whether their optical geometry is wrong[1]. What is clear from the Anderson et al. article is that the nonlinear relationships shown in each of these figures clearly violate Beer's law, and do not suggest that three or more hemoglobin species can be measured

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[1] While Anderson et al. contemplate a sample depth of .011 cm, which is within the range of sample depth contemplated by applicants, Anderson et al. note several "technical difficulties" inherent in the use of an integrating sphere in the paragraph spanning pages 180 an 181.

in whole blood, as required by the presently claimed invention. In fact, the nonlinear functional relationships presented in the Anderson et al. article actually suggest that attempting to do so would yield nonsense.

The Examiner combines the teachings of Anderson et al. with the Brown et al. patent, to allegedly render obvious claims in this application. As explained in the background portion of the present specification, the Brown et al. patent (U.S. Patent No. 4,134,678), is illustrative of complex prior art hemoglobinometers which force blood to obey Beer's law by hemolyzing and diluting the blood. Such hemolysis and dilution renders linear the functional relationship between optical density and hemoglobin concentration, thereby eliminating the deleterious effects of the nonlinear relationship which can occur with whole, undiluted blood. As explained above, this nonlinear relationship is illustrated in Anderson et al., and, contrary to the Examiner's contention, Anderson et al. fails to provide a solution to that problem.

Moreover, Anderson et al. deal with whole, undiluted blood, whereas the Brown et al. patent hemolyzes and dilutes the blood before spectrometering (see col. 13, line 57 through col. 14, line 1, and each independent claim). Thus, the two disclosures are completely incompatible, and are thus not properly combinable.

It should also be noted that in addition to Brown et al., other researchers in hemoglobinometry have concluded that the way to avoid the problematical nonlinear nature of the functional relationship between optical density and hemoglobin concentration

in hemoglobinometry (clearly illustrated by Anderson et al.), is to hemolyze the blood, dilute the blood, or both. For example, in addition to the Brown et al. patent, the Raffaele patent (U.S. Patent No. 4,013,417, filed July 31, 1975), requires hemolysis and dilution; the Siggaard-Andersen patent (U.S. Patent No. 4,308,029, filed May 5, 1980) requires chemical deoxygenation followed by hemolysis and dilution; the Johansen et al. patent (U.S. Patent No. 3,972,614, filed July 10, 1974), requires hemolysis by ultrasound; the Loretz patent (U.S. Patent No. 4,357,105, filed August 6, 1980), requires hemolysis and dilution; the Golias et al. patent (U.S. Patent No. 4,502,786, filed December 26, 1979), requires dilution; and the Frey patent (U.S. Patent No. 3,994,585, filed August 11, 1975), requires dilution. Each of these references are of record.

Each of these researchers (each of whom filed patent applications long after publication of the Anderson et al. article), avoided the known nonlinear functional relationship between optical density and hemoglobin concentration, by hemolyzing the blood, diluting the blood, or both. The only method that has been successful in spectrometering whole, undiluted blood to measure three or more constituent components, is applicants' own. The failure of these researchers and others to arrive at applicants' method is clearly illustrative of the nonobviousness of the presently claimed invention.

The Examiner also combines the Shibata reference with the teachings of Anderson et al. and Brown et al. to render claims 3

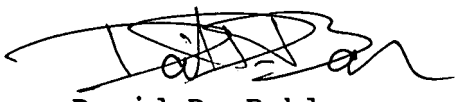
and 5 allegedly obvious. Applicants respectfully traverse this rejection.

First, applicants note that the Shibata et al. reference does not supply the above-noted deficiencies in the Anderson et al. teachings, and does not cure the incompatibility of the Anderson et al. and Brown et al. teachings. In addition, the purpose of the Shibata et al. reference is to overcome certain undesirable properties of photomultiplier tubes by more evenly distributing light over the face of a detector surface. This is achieved by using a light-diffusing plate, which in turn necessitates placing the detector close to the sample. Shibata et al. has nothing to do with whole-blood spectrophotometric measurements, and is therefore non-analogous art. In addition, absent applicants' disclosure, there is absolutely no motivation in the teachings of the prior art to apply the Shibata et al. structure to the combination of Anderson et al. and Brown et al.

In light of the foregoing amendments and points of discussion, applicants respectfully request the withdrawal of the rejection of claims 1-12, the allowance of these claims, and their passage to an early issue. Applicants believe the foregoing to be a full and complete response to the subject Office Action. Should the

Examiner believer that a personal discussion would be helpful, he is encouraged to contact the undersigned at the telephone number listed below.

Respectfully submitted,



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